

# WHY COMPOUND HORMONES? (FEMALE HRT)

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# INTRODUCTION

- Bryan Ziegler, PharmD/MBA
  - President/Clinical Compounding Pharmacist @ Moss Compounding
  - Clinical Adjunct Associate Professor – Univ. of S. Carolina Coll. Of Pharmacy
  - PCCA Hormone Therapy Specialist
- Moss Compounding Pharmacy
  - Full scale compounding pharmacy
    - Human and Veterinary compounding
    - Sterile and Non-sterile
    - Hazardous (Non-sterile only)



# MENOPAUSE: SYMPTOMS

- Irritability
- Memory loss
- Depression
- Nervousness
- Diminished sex drive
- Painful intercourse
- Urinary incontinence
- Heart palpitations

- Hot Flashes
- Hair loss
- Dry skin
- Sleep disturbances
- Night sweats
- Anxiety
- Vaginal Dryness
- Vaginal atrophy



**Night sweats and hot flashes are nature's way of lowering your heating bill so you can save more money for your retirement.**

ding (C4)



# The Seven Stages of Menopause



Itchy



Bitchy



Sweaty



Sleepy



Bloated



Forgetful



Psycho



# SYMPTOM RELIEF OPTIONS

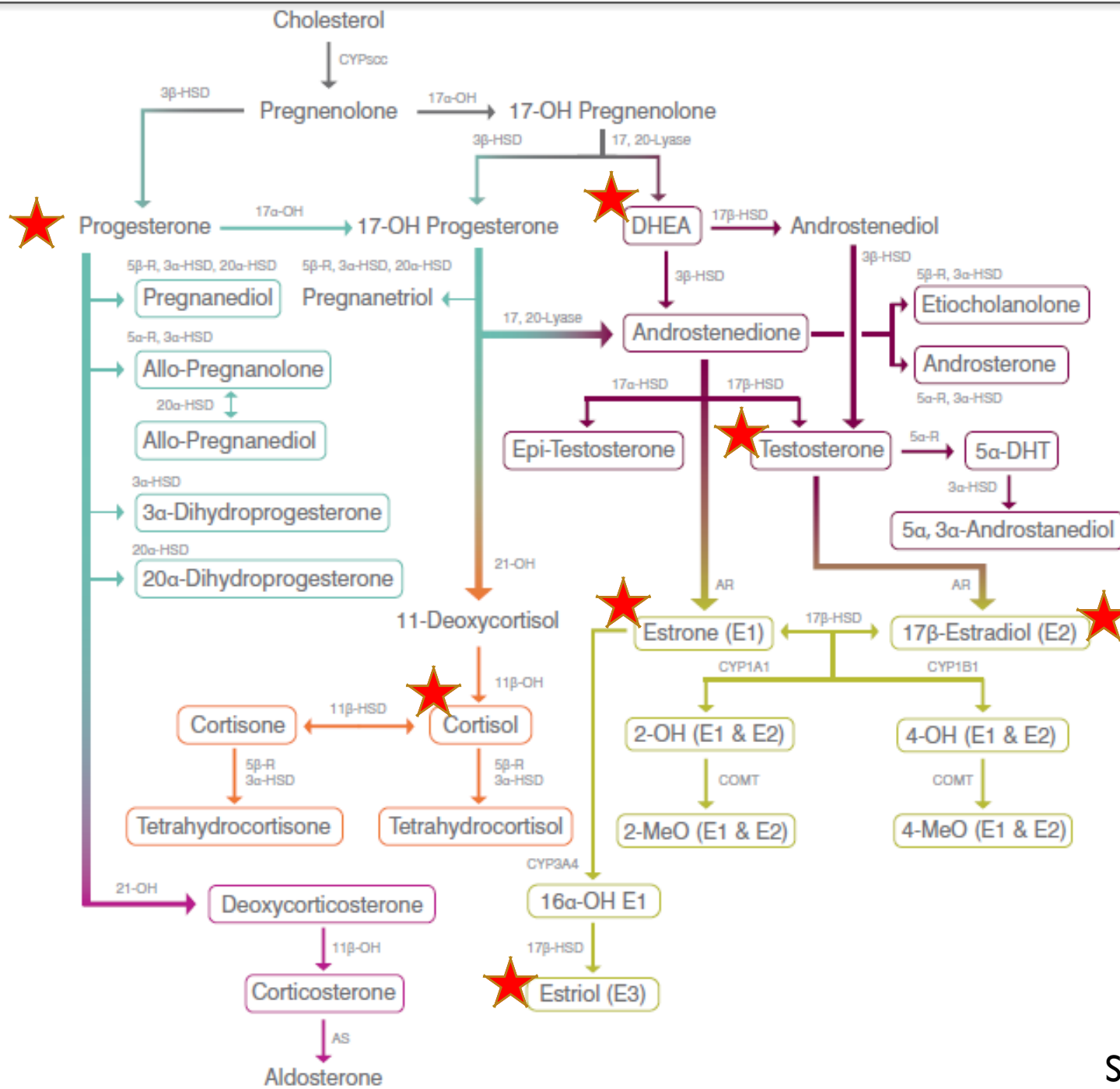
- Hormone Replacement Therapy (HRT)
  - Terms/Types
  - Risk/Benefit
    - What we know now
      - Estrogen - bio-identical options better, topical better than oral
      - Progesterone - bio-identical better results, different side effects
      - Testosterone - topical/sublingual/vaginal best ways to administer



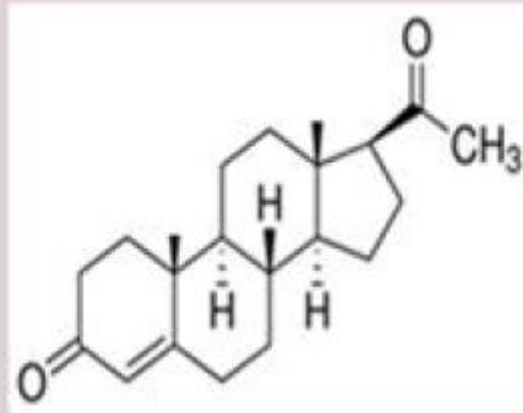
Key Terminology:

Term	Definition
Hormone Therapy	Treatment of diseases or underlying medication conditions with hormones obtained from endocrine glands or substances that simulate hormonal effects; encompasses both estrogen therapy and estrogen plus progestogen therapy, and may include natural, semisynthetic, or synthetic hormones.
Bio-identical Hormone Therapy	Treatment with medications that contain hormones that have the same chemical formula on a molecular level as those made naturally in the body.
Natural	Derived from plant or animal sources.
Semisynthetic	Produced by chemical manipulation of natural materials.
Synthetic	Produced in a laboratory.
Compounding	Preparing, mixing, assembling, altering, packaging, and labeling of a drug or device in accordance with a licensed practitioner's prescription. A key component of compounding and one that differentiates it from manufacturing is that it occurs in the presence of the practitioner/patient/pharmacist relationship.
Progesterone	Refers to a single molecular structure that is identical to the progesterone molecule that the body makes, also referred to as P4.
Progestogen	The category of hormone molecules (natural and synthetic) that act like progesterone in the uterus.
Progestin	Generally refers to synthetic progestogens.

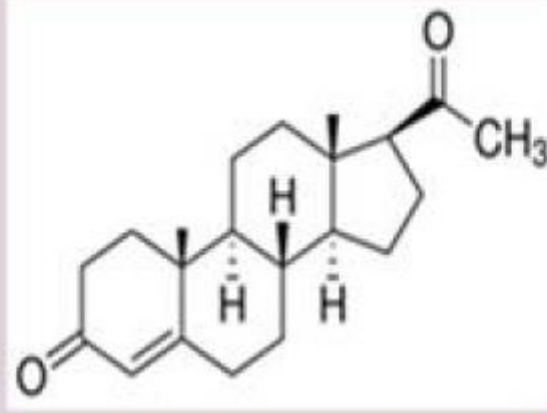




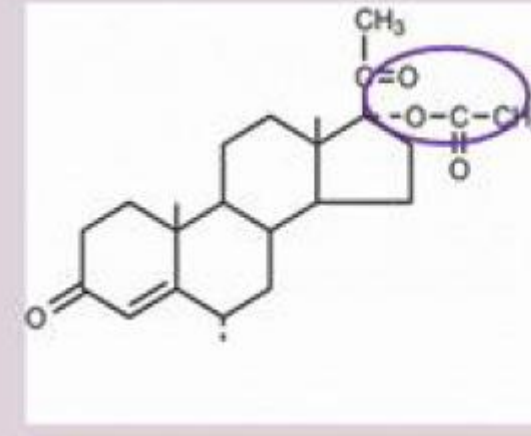
## Chemical Structures Explain It All



Progesterone-  
Bioidentical



Physiological  
Progesterone



Medroxyprogesterone  
Acetate

**Bioidentical Hormone Therapy are what many women are looking for when they say they want “natural hormone therapy”.**

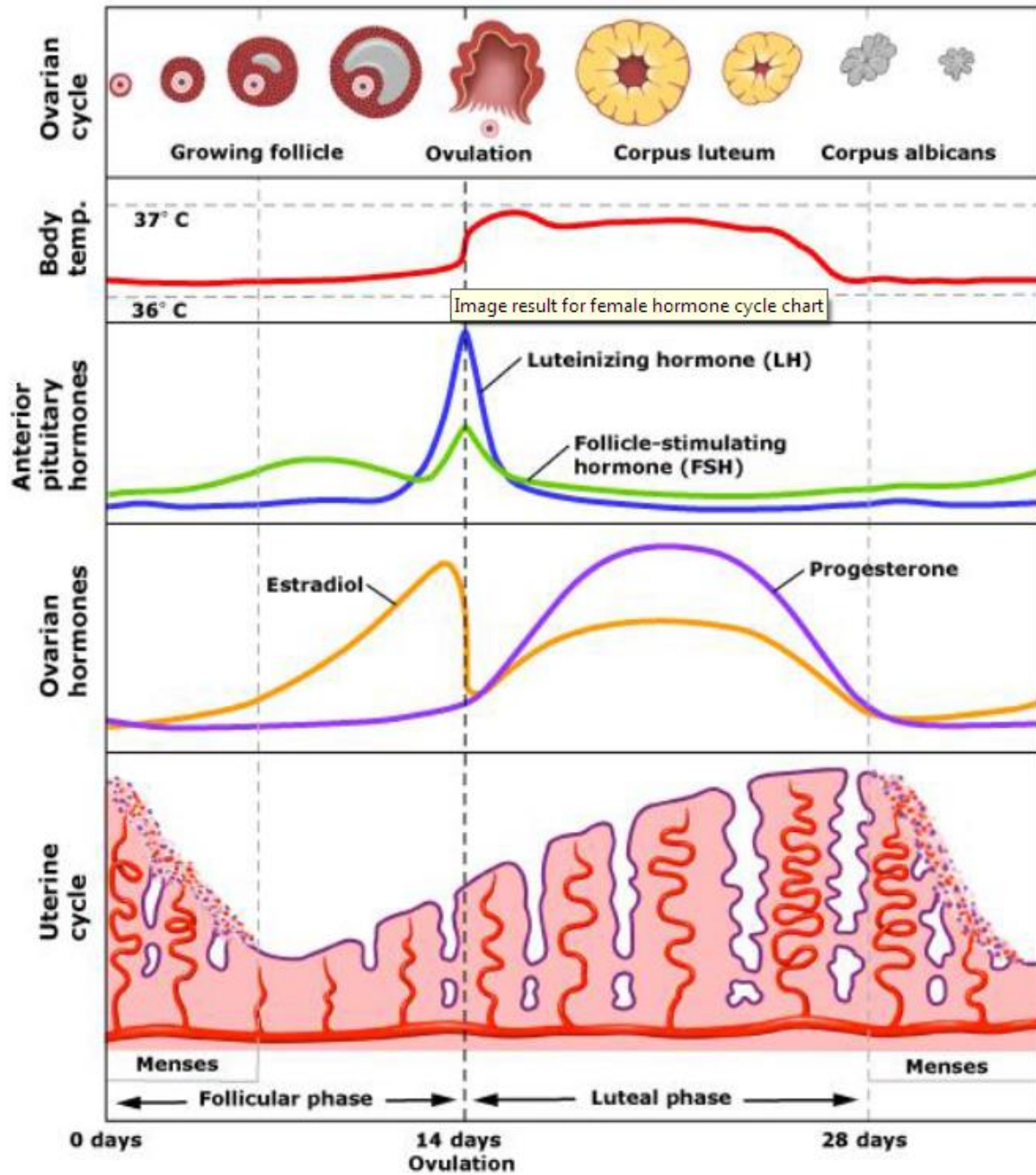




# NATURAL PROGESTERONE EFFECTS NOT SEEN WITH PROGESTINS

- ▶ Helps balance estrogen
- ▶ Leaves the body quickly
- ▶ Improves sleep
- ▶ Natural calming effect
- ▶ Lowers high blood pressure
- ▶ Helps the body use and eliminate fats
- ▶ Lowers cholesterol
- ▶ Increases scalp hair
- ▶ Helps balance fluids in the cells
- ▶ Increases the beneficial effects of estrogen on BV
- ▶ Increases metabolic rate
- ▶ Natural diuretic
- ▶ Natural antidepressant
- ▶ Is anti-inflammatory
- ▶ Stimulates the production of new bone
- ▶ Enhances the action of thyroid hormones
- ▶ Improves libido
- ▶ Helps restore proper cell oxygen levels
- ▶ Induces conversion of E1 to the inactive E1S form
- ▶ Promotes Th2 immunity
- ▶ Is neuroprotective, promoting myelination





# WHY COMPOUNDING?

Compounding offers an alternative solution for patients when commercial products are ineffective, impractical, or unavailable

Compounding allows the prescriber, pharmacist and other health care providers to use their clinical skills to design a patient-specific therapy to address specific patient needs



# WHY USE A COMPOUNDED HRT?

- Bio-identical ingredients
- Wide variety of dosage forms
- Individualized, Customizable dosage forms
  - Unlimited combinations/strengths available
  - Allows for improved compliance opportunities
- Avoid unwanted ingredients (allergies and/or adverse events)
  - Ex. Removal of propylene glycol with vaginal preps
  - Ex. Peanut allergy with Prometrium





## UNIQUE DOSAGE FORMS - COMPOUNDED HRT

Creams

Topical

Vaginal

Gels

Ointments

Capsules – IR, TR

Troches

Suppositories

# KEY POINT – WHAT HAVE I LEARNED....

- No two women are alike
  - Hormone levels fluctuating/changing
  - Symptoms are different
  - Other health conditions
  - Risk/Benefit
- Customization of therapy can be very beneficial to addressing symptoms and achieving desired results
- Thus....cookie-cutter approach to treatment typically doesn't produce the desired results.



# CURRENT MENOPAUSE HRT RECOMMENDATIONS

- HT remains the most effective therapy for vasomotor symptoms and urogenital atrophy <sup>1,2</sup>
- Other menopause-related complaints, such as joint and muscle pain, mood swings, sleep disturbances, and sexual dysfunction (including reduced libido) may improve with HT. <sup>1,2</sup>
- Administration of individualized HT (including androgenic preparations when appropriate) may improve both sexuality and overall quality of life. <sup>2</sup>



# CURRENT MENOPAUSE HT RECOMMENDATIONS

- HT should be part of an overall strategy including lifestyle recommendations regarding diet, exercise, smoking cessation, and safe levels of alcohol consumption.<sup>1,2</sup>
- HT **must be individualized and tailored** according to symptoms and the need for prevention, as well as personal and family history, results of relevant labs, and the woman's preferences & expectations. <sup>1,2</sup>
- Risk and benefits of HT differ for women during the menopause transition compared to those of older women. <sup>1,2</sup>





# CURRENT MENOPAUSE HT RECOMMENDATIONS

- Dosage should be titrated to the **lowest effective dose**.<sup>1,2</sup>
- There are **no reasons to place mandatory limitations on duration** of HT. <sup>1,2</sup>
- Wide range of hormonal products and routes of administration, with potentially different risks and benefits. Thus, the term 'class effect' is confusing and inappropriate. However, evidence regarding differences in risks and benefits between products is limited. <sup>2</sup>



# CURRENT MENOPAUSE HT RECOMMENDATIONS

- Spontaneous or iatrogenic menopause before age 45 (and particularly before age 40) = higher risk for CV disease & osteoporosis and possibly increased risk of dementia and affective disorders. HT may reduce symptoms and preserve bone density and is advised at least until the average age of menopause (51).<sup>1,2</sup>
- At least annual consultation including PE, updated medical & family Hx, relevant labs/imaging, recommended. Continue mammogram and pap smear on regular schedule.<sup>1,2</sup>
- Lower doses of HT may reduce symptoms and maintain QOL for women. However, long term data on lower doses regarding fracture or cancer risks and CV implications are still lacking.<sup>2</sup>



# COMPOUNDED HORMONE THERAPY

- *"...consider compounded HT if women cannot tolerate a government-approved therapy for reasons such as allergies to ingredients or for a dose or formulation not currently available in government-approved therapies."*

- North American Menopause Society

Position Statement 2017

(*Menopause*, Vol 24, No. 7, 2017)



# CONCERNS WITH COMPOUNDED HRT

## ISSUE RAISED

- Lack of quality control with preparations

## RESPONSE

- We compound with USP approved ingredients (same as drug manufacturers) that are acquired from FDA-approved suppliers
- We conduct random testing of preparations to confirm potency and consistency in compounding process



# TOPICAL HRT COMPOUND PACKAGING



# CONCERNS WITH COMPOUNDED HRT

## ISSUE RAISED

- Lack of scientific efficacy and safety data

## RESPONSE

- Large scale clinical trials for compounded medications are not available because of funding limitations and because of individualization of dosing
- Individualization allows for the lowest effective dose to be administered – which is the current recommendation for safe use of HRT



# CONCERNS WITH COMPOUNDED HRT

## ISSUE RAISED

- Minimal government regulation and monitoring

## RESPONSE

- Compounding pharmacies are regulated by state boards of pharmacy.
- All state and federal legal requirements for a compounded prescription are met
- Compounding pharmacies do not have to comply with the large scale manufacturing requirements of drug companies because they are compounding patient-specific preparations and not mass scale distribution.



## FDA-APPROVED INDICATIONS

### **Vasomotor symptoms**

Hormone therapy has been shown in double-blind RCTs to relieve hot flashes<sup>23</sup> and is approved as first-line therapy for relief of menopause symptoms in appropriate candidates.

### **Prevention of bone loss**

Hormone therapy has been shown in double-blind RCTs to prevent bone loss, and in the WHI, to reduce fractures in postmenopausal women.<sup>24,25</sup>

### **Premature hypoestrogenism**

Hormone therapy is approved for women with hypogonadism, POI, or premature surgical menopause without contraindications, with health benefits for menopause symptoms, prevention of bone loss, cognition and mood issues, and in observational studies, heart disease.<sup>26-31</sup>

### **Genitourinary symptoms**

Hormone therapy has been shown in RCTs to effectively restore genitourinary tract anatomy, increase superficial vaginal cells, reduce vaginal pH, and treat symptoms of vulvovaginal atrophy (VVA).<sup>32</sup>

### **Key point**

- Hormone therapy is approved by FDA for four indications: bothersome VMS; prevention of bone loss; hypoestrogenism caused by hypogonadism, castration, or POI; and genitourinary symptoms.

POI =Primary Ovary  
Insufficiency



## Contraindications to Hormone Therapy

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No absolute contraindications of hormone therapy have been established. However, HT is relatively contraindicated in certain clinical situations, such as patients with the following findings:

- A history of breast cancer
- A history of endometrial cancer (see Uterine Cancer and Endometrial Carcinoma)
- Porphyria
- Severe active liver disease
- Hypertriglyceridemia
- Thromboembolic disorders (see Deep Venous Thrombosis and Pulmonary Embolism)
- Undiagnosed vaginal bleeding (see Dysfunctional Uterine Bleeding)
- Endometriosis
- Fibroids

Note that many clinicians do not prescribe HT for women with a previous history of breast or endometrial cancer.



*Kaur K, Lucidi R, et al. Menopause Hormone Replacement Therapy: Practice Essentials, Overview, Symptoms and Effects of Menopause. Medscape January 4, 2018. Accessed March 20, 2018.*

# BIO-IDENTICAL HRT OPTIONS

Drug	Dosages Available	Typical Dosing Recommendation	Notes/Comments
Estradiol tablets	0.5mg, 1mg, 2mg	1 tab <u>po</u> QD	Impact of 1 <sup>st</sup> pass effect with oral dosing
Estradiol Patch (various)	See next page for table	Apply either twice weekly or weekly	<u>Alora</u> , <u>Climara</u> , <u>Minivelle</u> , <u>Vivelle Dot</u>
Estradiol Vaginal cream ( <u>Estrace</u> )	0.01% (0.1mg/gm)	2-4gm QD x 1-2weeks, 1-2gm QD x 1-2 weeks, 1gm 3 x week	Cost = ~\$300/tube Contains Propylene glycol
Estradiol cream (compound)  +/- Vitamin E 200IU	Various (0.1mg/0.5mL)	0.5mL <u>pv</u> QD x 1-2 weeks, then 2-3 x weekly prn	Transdermal or Transvaginal use <u>*Propylene Glycol free*</u>
<u>Estriol</u> Vaginal Cream (compound)	Various  Typical = 1mg/0.5mL	Insert vaginally nightly for 2 weeks, Monday & Thursday for 2 weeks, then PRN	Weaker estrogen with protective effects (particularly in combo with Estradiol)  Great option for vaginal symptoms.  Approved and widely used in Europe. No FDA approved commercial product in US.



# BIO-IDENTICAL HRT OPTIONS (CONT)

Drug	Dosages Available	Typical Dosing Recommendation	Notes/Comments
Bi-Estrogen cream <b>(compound)</b> – Estriol (E3)/Estradiol (E2)	Various (80:20); (50:50) typical ratios	Typically applied QD to BID (split dose) to upper inner arm or thigh.	Transdermal or Transvaginal application
Estradiol Vaginal (Femring/Estring)	0.05 or 0.10mg (Femring) 0.0075mg (Estring)	Inserted vaginally for 90 days	Systemic level effect (Femring) Local effect (Estring)
Estradiol vaginal tablet (Vagifem, Yuvaferm)	0.01mg	1 vaginally qd x 2 weeks, then 2x/week	
Estradiol vaginal insert (Imvexxy®)	0.004mg (4mcg), 0.01mg (10mcg)	1 vaginally qd x 2 weeks, then 2x/week	Approved for VVA, dyspareunia
Estradiol Transdermal gel (Divigel, Elestrin, EstroGel)	Divigel 0.1% – 0.25, 0.5, 1mg (0.25 – 1gm) Elestrin – 0.52mg/pump (0.87gm) EstroGel – 0.75mg (1.25gm)	QD to various sites (see individual products)	Alcohol-based gels (topical use only)  Hormone Transfer concerns (arm application)
Estradiol Transdermal spray (Evamist)	1.53mg/spray	1 spray per day, adjust up to 3 sprays/day PRN	Alcohol-based spray  Hormone Transfer concerns (arm application)
Estradiol valerate oil injection (Delestrogen)	10mg/mL; 20mg/mL; 40mg/mL	10-20mg IM q4wks PRN	
Estradiol cypionate oil injection (Depo-Estradiol)	5mg/mL	1mg – 5mg IM q3-4wks PRN (short-term) 1.5mg-2mg IM q4wk	



# BIO-IDENTICAL HRT OPTIONS (CONT)

Drug	Dosages Available	Typical Dosing Recommendation	Notes/Comments
Testosterone Sublingual (compound)	0.5mg, 1mg, 2mg	1 SL QD to BID (early morning and mid-afternoon)	Transdermal options preferred to SL
Testosterone cream (compound)  (transdermal gel also available)	1% (1mg/0.1mL), others as needed	Initial: 0.1mL (1mg) applied QD	Transdermal or Transvaginal application (Vaginal application helpful to improve libido)
Progesterone TR Capsule (compound)	25mg, 50mg, 75mg, 100mg, 125mg, 150mg, 200mg	1 <u>po</u> QHS (30 min – 1hr before bedtime)	Good option for early sleep awakening
Progesterone Capsule ( <u>Prometrium</u> )	100mg, 200mg	1 <u>po</u> QHS (30 min – 1hr before bedtime)	Contraindicated in peanut allergy  Immediate release form Helps initiate sleep
Progesterone cream (compound)	0.5% - 5% (5mg/mL – 50mg/mL)	Applied QD to BID (split dose)	Transdermal or Transvaginal application



# BIO-IDENTICAL HRT OPTIONS (CONT)

Drug	Dosages Available	Typical Dosing Recommendation	Notes/Comments
DHEA cream (compound)	1-10 mg/mL	Apply 0.5mL QD	Transdermal or Transvaginal application
DHEA Capsules (IR & SR) (compound)	2.5mg, 5mg, 7.5mg, 10mg	1 po QD	
DHEA tablets	5mg	1-2 po QD	Available OTC
DHEA Suppositories (Compound)	3.25mg, 6.5mg, 13mg	1 <u>pv</u> HS	
Intrarosa <sup>®</sup> (Prasterone) Vaginal inserts	6.5mg	1 <u>pv</u> QHS	Aka DHEA Indicated for moderate to severe dyspareunia



# OTHER HRT OPTIONS (NOT BIO-IDENTICAL)

Drug	Bio-Identical (Y/N)	Strengths Available	Notes/Comments
Conjugated Equine Estrogens ( <u>Premarin</u> <sup>®</sup> , <u>Enjuvia</u> <sup>®</sup> )	No	Tablet: 0.3mg, 0.625mg, 0.9mg, 1.25mg ( <u>Enjuvia</u> only 0.625 & 1.25mg)  <u>Vag Cream (Premarin)</u> : 0.625mg/gm	<u>Vag cream</u> : \$370/tube`
Esterified Equine Estrogens ( <u>Menest</u> <sup>®</sup> ) tablets	No	0.3mg, 0.625mg, 1.25mg, 2.5mg	From pregnant mares, predominantly <u>Estrone</u>
<b>Progesterone/Progestin Only</b>			
Provera <sup>®</sup> (Medroxyprogesterone acetate) tablets	No	2.5mg, 5mg, 10mg	Caution using this option. Many adverse events with this option Many detrimental effects from WHI linked to this drug.



# OTHER HRT OPTIONS (+/- BIO-IDENTICAL)

Drug	Bio-Identical (Y/N)	Strengths Available	Notes/Comments
<b>Testosterone Only</b>			
None available commercially			Compound options only available for females
<b>Combination Products</b>			
<u>Prempro</u> ® (Conjugated Equine Estrogens/Medroxyprogesterone acetate) tablets	No	0.3mg/1.5mg 0.45mg/1.5mg 0.625mg/2.5mg 0.625mg/5mg	Caution using this option.
<u>Premphase</u> ® (Conjugated Equine Estrogens/Medroxyprogesterone acetate) tablets	No	0.625mg (CE) – day 1-14 0.625mg/5mg day 15-28	Caution using this option.
<u>Estratest</u> ® (Esterified Equine Estrogens/Methyltestosterone) tablet	No	Reg – 1.25mg/2.5mg HS – 0.625mg/1.25mg	From pregnant mares, predominantly Estrone
<u>Duavee</u> ® (Conjugated equine estrogen + bazedoxifene) tablet	No	0.45mg/20mg	CEE + Estrogen agonist/antagonist
<u>Activella</u> ® (Estradiol/Norethindrone acetate) tablet	Estrogen = Yes Progestin = No	0.5mg/0.1mg per day 1mg/0.5mg per day	
<u>Angeliq</u> ® (Estradiol/drospirenone) tablet	Estrogen = Yes Progestin = No	0.5mg/0.25mg per day 1mg/0.5mg per day	
<u>FemHRT</u> ® (Ethinyl Estradiol/Norethindrone acetate) tablet	No	2.5mcg/0.5mg 5mcg/1mg	
<u>Bijuva</u> ® (Estradiol/Progesterone) cap	Estrogen = Yes Progest = Yes	1mg/100mg	
<u>Climara Pro</u> ® patch (Estradiol/levonorgestrel)	Estrogen = Yes Progestin = No	0.45mg/0.015mg (daily dose)	Once weekly patch
<u>Combipatch</u> ® (Estradiol/Norethindrone acetate)	Estrogen = Yes Progestin = No	0.05mg/0.14mg (daily) 0.05mg/0.25mg (daily)	Twice weekly patch

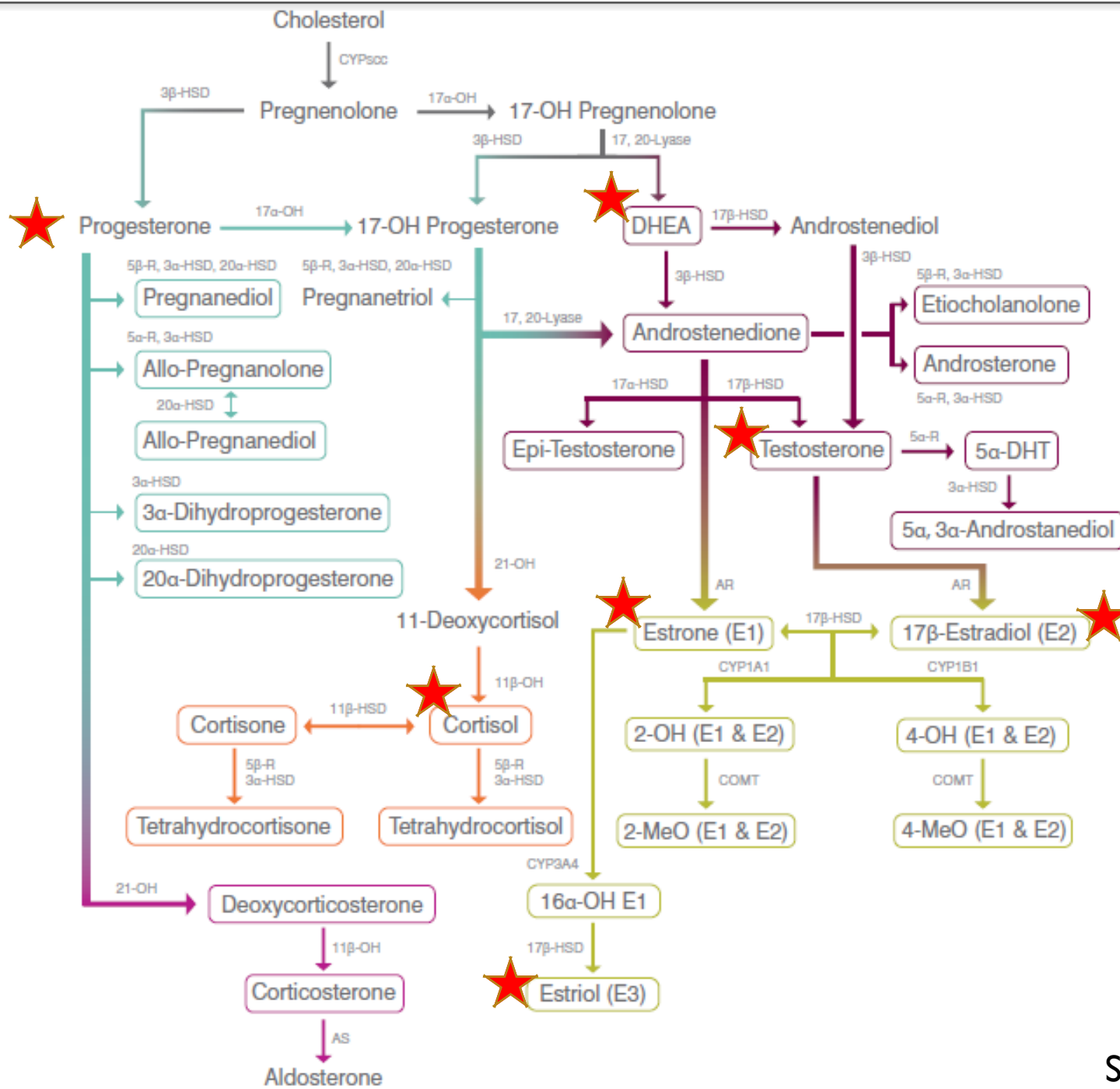


# HOW TO PRESCRIBE COMPOUNDED HRT

- Include the word “Compound” or “Compounded” on Rx
- Estrogen Component
  - Estriol (E3)
  - Estradiol (E2)
  - Estriol (E3) + Estradiol (E2) = Bi-estrogen
    - Indicate ratio of Bi-estrogen mix + strength + SIG
    - Ex. Bi-estrogen (80:20) 1mg topically QD
      - Ratio is (E3:E2), thus 80% E3 and 20% E2 in this compound
- Progesterone
  - Oral: “Compounded Progesterone”; TR or SR \_\_\_mg
- Testosterone
- DHEA
- ***Can be ordered as separate dosage forms or combined***







# HOW TO PRESCRIBE COMPOUNDED HT

- Example of combined HRT compound Rx:

Bi-estrogen (80:20) 1mg  
Progesterone 40mg  
Testosterone 2mg

} per mL cream

Qty: QS for 1month

SIG: Apply 0.5mL topically or vaginally QD on days 1-25 of the month

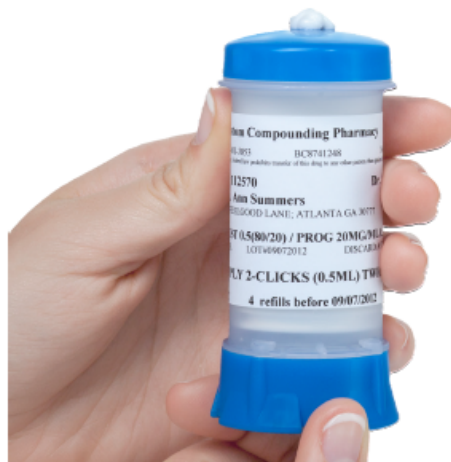




MOSS COMPOUNDING  
PHARMACY

# TESTOSTERONE REPLACEMENT

## TOPICAL CREAM



OR



### TOPI-CLICK 35

0.25mL per click  
Typical dose = 0.5mL

0.5mg/0.5mL = \$40 (15mL)  
1mg/0.5mL = \$48 (15mL)

### TOPI-CLICK MICRO

0.05mL per click  
Typical dose = 0.1mL (1mg)

1% (10mg/mL) pricing  
3mL = \$38  
6mL = \$50

Typical SIG: Apply 1mg topically QD

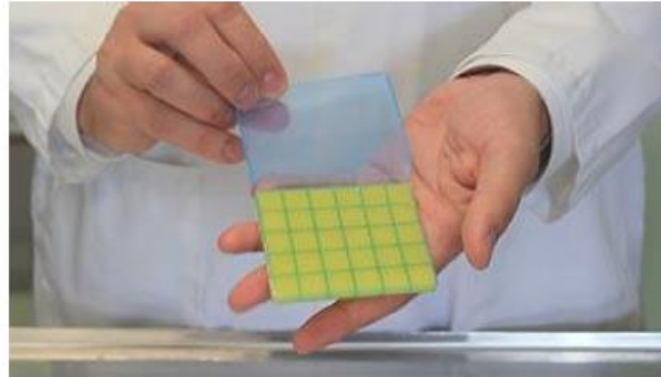




MOSS COMPOUNDING  
PHARMACY

# TESTOSTERONE REPLACEMENT

## SUBLINGUAL TROCHES (GELATIN)



### TYPICAL DOSES

1mg #30 count = \$60  
2mg #30 count = \$65  
4mg #30 count = \$70

### FLAVORS

Strawberry, Peach  
Pina Colada, Raspberry,  
Cran-Raspberry, Apple,  
Creme De Menthe,  
Marshmallow,  
Banana Creme, & more!

Typical SIG: Dissolve 1 troche under tongue or buccal cavity QD





MOSS COMPOUNDING  
PHARMACY

# ESTRIOL VAGINAL CREAM 1MG/0.5ML

Patient convenience.  
Less mess.  
Affordable Price.  
Bio-Identical Treatment Option.



## TOPI-CLICK PERL

1st month (9mL) = \$48  
Maintenance (8mL) = \$45\*  
\*2 month supply

OR



## UNIT DOSE

1st month (9mL) = \$56  
Maintenance (4mL) = \$28

## Benefits of Compounded Vaginal creams:

- **Customizable dosing options available**
- **Ease of use and dosing** - We pre-fill disposable vaginal applicators for consistent dosing and no cleaning of applicators afterwards.
- **Lower volume of cream** - we typically concentrate hormone creams to 0.5mL doses (~0.5gm). This is less cream (ie. less messy) than commercial products, which may require 1 - 2 gm per dose.
- **Propylene glycol free products** - our compounds contain glycerin, which is moisturizing to vaginal tissue
- **Lower price tag** - a more affordable option for patients facing high copays or no insurance.



## Prescribing Estriol Vaginal Cream:

Typical SIG: 0.5mL (=1mg dose) vaginally QHS for 14 nights,  
then Twice weekly for vaginal dryness/atrophy.

Quantity: Initial therapy = 9mL (28 days supply)  
Maintenance = 4mL (28 days supply)

\*Note: Minimum Quantity for Topi-click PERL packaging is 8mL

\*\*Note: Estriol 1mg vaginal cream is a comparable dose to Estrace or  
Premarin Vaginal cream

# MOSS COMPOUNDING PHARMACY – HOW WE CAN HELP!

- Services
  - Hormone evaluations/consultations
  - Hormone therapy recommendations
  - Medication compounding
  - Hormone therapy monitoring
  - Saliva, Blood spot, urine testing



# KEY POINT – WHAT HAVE I LEARNED....

*ELSE*

- No two women are alike
  - Hormone levels fluctuating/changing
  - Symptoms are different
  - Other health conditions
  - Risk/Benefit
- Customization of therapy can be very beneficial to addressing symptoms and achieving desired results
- Thus....cookie-cutter approach to treatment typically doesn't produce the desired results.
- ***Clinically treating and managing hormone therapy patients takes time.***



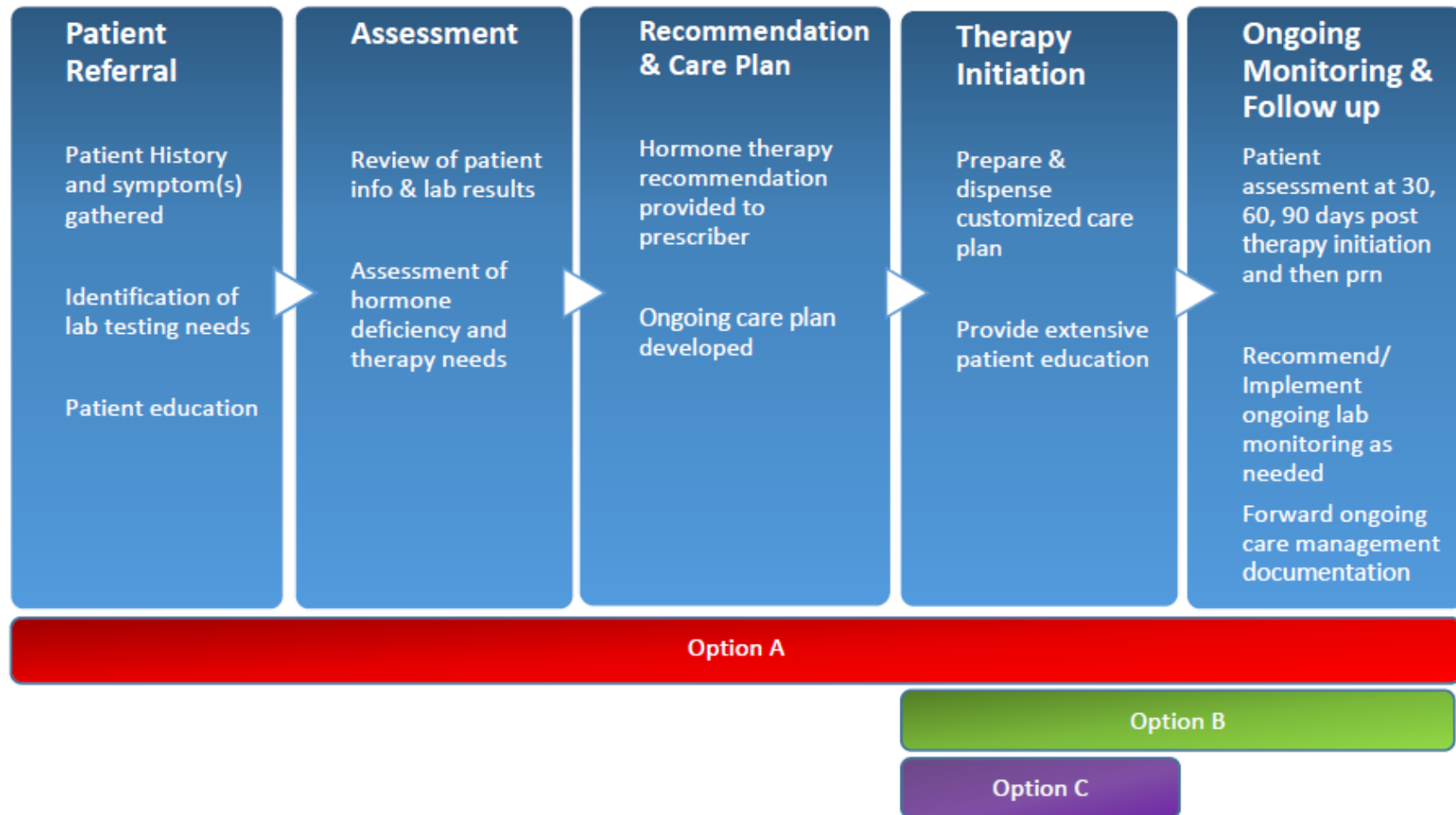
## Collaborative Hormone Therapy Management Service

We have multiple ways in which we can assist you:

Option A: Comprehensive Hormone Therapy Care

Option B: Follow up and Ongoing Monitoring for Hormone Therapy

Option C: Dispensing of Customized Hormone Therapy Prescriptions





# FEEDBACK FOR FUTURE TOPICS IN HRT

- Female sexual dysfunction
- Cortisol and the HPA Axis – how it impacts hormones
- How to prescribe compounded HRT
- Options in hormone level testing – Saliva, Serum, Urine, Blood spot
- Other vaginal issues: Vulvodynia, Endometriosis, Dyspareunia, Atrophy, Lichen sclerosis
- Recurrent BV and Non-candida albicans infection treatment



# UPCOMING EVENTS

Join us the 4th Tuesday of every month  
for new presentations

## UPDATES ON LOW DOSE NALTREXONE (LDN)

TUESDAY, SEPT 28 @ 6:30 – 7:00 PM



FOR DETAILS - VISIT THE **PRESCRIBER LEARNING CENTER @**  
[www.mosscompounding.com](http://www.mosscompounding.com)



# QUESTIONS?

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